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provided herein for the Examiner's consideration in support of applicant's arguments traversing the allegation of lack of utility, summarized below.

REJECTION OF CLAIMS 1, 3, 4 AND 11-16 UNDER 35 U.S.C. §101

Claims 1, 3, 4 and 11-16 are rejected under 35 U.S.C. §101 as allegedly not being supported by either a specific utility or a well established utility. It is alleged that the combinatorial set of compounds prepared by the claimed methods are themselves the subject of research, and therefore lack utility. Applicant respectfully traverses this rejection.

As described in detail in the amendment, mailed August 27, 2001, the instant claims are supported by a specific asserted utility and a well established utility. The enclosed references support the well established utility of the combinatorial libraries produced by the instantly claimed methods.

Utility of the claimed subject matter

The Office Action alleges that instant claims 1, 3, 4 and 11-26 are not supported by either a specific asserted utility or a well established utility. Applicant respectfully disagrees.

Specific asserted utility

It is alleged in the Office Action that the specification discloses that the compounds (oligonucleotides) are useful as drugs, which is not specific. In fact, the specification discloses that the compounds prepared by the claimed methods are useful in antisense and triplex DNA therapy (see, *e.g.*, the specification at page 2, lines 15-16 and page 14, lines 14-19).

The Office Action alleges that the specification does not identify the compounds which would be useful as drugs. It is respectfully submitted that such identification is not necessary. One of ordinary skill in the art would be able to determine, using standard assays known to those of skill in the art, which compounds of a library prepared by the instantly claimed methods would have the requisite biological activity. The biological activity required is a function of the disease, disorder or symptom to be treated. Thus, one of

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ordinary skill in the art would be able to readily determine, for a given disease, disorder or symptom, which compounds of a given library possess the required biological activity for that disease, disorder or symptom.

It is further alleged that there "is no basis in the specification upon which to conclude that *any* of the compounds encompassed by the library are, or will turn out to be, biologically active after testing," and that the "nucleic acid library prepared by the claimed method would require further research to identify useful oligonucleotides." It is respectfully submitted that the claimed method could be used to prepare libraries containing, in addition to new compounds, known antisense/triplex DNA agents. Therefore, these libraries would contain compounds which are biologically active. No further research would be required to determine that these libraries contained identifiable useful oligonucleotides. Furthermore, as noted above, one of skill in the art would be able to readily determine, using standard assays, which compounds possess requisite activity as antisense agents or for formation of triplex DNA, *e.g.*, for treatment of a given disease, disorder or symptom.

Moreover, the Office Action has not set forth any reasons for doubting the asserted utility. It was well known in the art, at the time the application was filed, that oligonucleotide analogs are useful as antisense and triplex DNA agents. The instantly claimed methods provide methods for the preparation of such compounds. The instantly claimed methods are applicable to the preparation of a wide variety of oligonucleotide analogs, including known antisense and triplex DNA agents. Given this applicability of the methods, there is no reason for the Office to doubt the asserted specific utility.

Well established utility

It is further alleged in the Office Action that the combinatorial libraries produced by the instantly claimed methods are not supported by a well established utility. Applicant respectfully disagrees.

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As noted in the Office Action, "a well established utility is a specific utility which is well known, immediately apparent and implied by the specification based on the disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art." As described in detail above, the combinatorial libraries prepared by the instantly claimed methods contain, *e.g.*, oligonucleotide analogs. It was well known at the time the application was filed that oligonucleotide analogs have utility as antisense or triplex DNA agents. See, *e.g.*, Uhlmann *et al.* (1990) *Chem. Rev.* 90:543-584 and Beaucage *et al.* (1993) *Tetrahedron* 49:6123-6194, cited in the application (copies enclosed).

Moreover, the libraries produced by the instantly claim process have utility in screening for compounds that are useful as antisense agents. Such libraries contain oligonucleotides and/or oligonucleotide analogs. These libraries were well known to those of skill in the art at the time the application was filed to have utility in screening for antisense agents.

It is further alleged in the application that "the compounds of the claimed libraries are not recognizable as analogous to compounds with a recognized pharmacological (or other) activity." Applicant notes that instant claims 4 and 11-16 are directed to processes for generating combinatorial libraries, not to combinatorial libraries themselves. Moreover, the compounds of the libraries produced by the instantly claimed methods are, *e.g.*, oligonucleotide analogs. As noted above, such compounds are well known to possess activity as antisense or triplex DNA therapeutic agents. Furthermore, the instantly claimed processes may be used to prepare known oligonucleotide analogs, among other compounds. Therefore, contrary to the assertion of the Office Action, data as to the activity of the compounds of the libraries produced by the instantly claimed methods is not required to establish the utility of instant claims 4 and 11-16 because some of the compounds that may be prepared by the methods are known to have antisense and triplex DNA activity.

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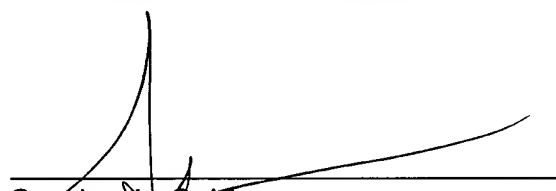
Applicant respectfully requests reconsideration and removal of this rejection.

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In view of the above, reconsideration and allowance of the application is respectfully requested.

Respectfully submitted,
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